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Water polymers in L-alanyl-L-methionine hemihydrate

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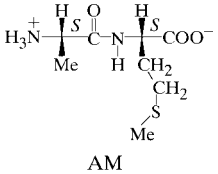
The side chains of L-alanyl-L-methionine hemihydrate, $C_8H_{16}N_2O_3S\cdot0.5H_2O$, form hydrophobic columns within a three-dimensional hydrogen-bond network that includes extended polymers of cocrystallized water molecules and $C^{\alpha}-H\cdots S$ interactions.

Comment

The crystal structure of L-Val-L-Ala (VA; Görbitz & Gundersen, 1996) was the first example of nanotube formation by such a small molecule. Subsequently, the reteroanalogue L-Ala-L-Val (Görbitz, 2002) and a series of other dipeptides with L-Ala, L-Val and L-Ile residues (Görbitz, 2003*b*) were found to form structures very similar to VA, differing only in the way that side chains partly fill the channels along the hexagonal axes, which translates directly to pore size.

To investigate whether crystallization in the VA class is compatible with dipeptides incorporating unbranched side chains (apart from the methyl group of L-Ala), crystallization and structure determination have been carried out for L-Met-L-Ala (MA) and L-Ala-L-Met (AM). The structure of MA is indeed closely related to the VA class, but with seven molecules in the asymmetric unit (Görbitz, 2003*a*). The crystal structure of $AM\cdot0.5H_2O$ is discussed here.



AM

The asymmetric unit of $AM\cdot0.5H_2O$, containing two peptide molecules and one water molecule, is shown in Fig. 1. There are no signs of any kind of disorder, and bond lengths and angles are normal. Peptide molecule *A* has an elongated main-chain conformation, in which the carboxylate group is coplanar with the N atom of the peptide bond (Table 1). The L-Met side chain has an unusual *gauche*+, *trans*, *trans* conformation for χ^1, χ^2 and χ^3 (N2*A*—C4*A*—C5*A*—C6*A*, C4*A*—C5*A*—C6*A*—S1*A* and C5*A*—C6*A*—S1*A*—C7*A*, respectively), which has been found previously only for D-Ala-L-Met (in the racemate; Stenkamp & Jensen, 1974; Guillot *et al.*, 2001), for one of the two side chains in cyclo(L-Met-L-Met) (Valle *et al.*, 1990) and for *N*-formyl-L-Met (Chen & Parthasarathy, 1977).

The main chain of peptide molecule *B* differs from that of *A* mainly in the carboxylate-group orientation defined by the N2*B*—C4*B*—C8*B*—O2*B* torsoin angle [−57.8 (2)°]. The side-chain *gauche*− rotamer for χ^1 (N2*B*—C4*B*—C5*B*—C6*B*) and the *trans* rotamer for χ^3 (C5*B*—C6*B*—S1*B*—C7*B*) are both quite common, but the *gauche*+ orientation for χ^2 (C4*B*—C5*B*—C6*B*—S1*B*) is very rare, and the *gauche*−, *gauche*+, *trans* combination for χ^1, χ^2 and χ^3 yields a conformation that has not been observed previously for any of the amino acids or peptides in the Cambridge Structural Database (CSD; Allen & Motherwell, 2002).

The packing diagram in Fig. 2 shows that even though some features are shared, like the aggregation of side chains into hydrophobic columns, AM is clearly not a member of the VA class. As was also evident from the $P2_12_12_1$ space group, AM lacks hexagonal symmetry, and furthermore, the open channels at the center of each hydrophobic column are missing. In the VA class, these channels are either empty or filled non-stoichiometrically with solvent molecules that can be removed by drying, with complete retention of the peptide scaffold (Görbitz & Gundersen, 1996; Görbitz, 2002). The cocrystallized solvent water molecules of AM are located close to the twofold screw axes parallel to the short 5.0809 (2) Å *a* axis; these molecules form an integral part of the hydrogen-bond network and cannot be removed by drying without destroying the crystal. Hydrogen bonds between water molecules give rise to polymers along the *a* axis that are surrounded by peptide *B* molecules, as seen in Fig. 3. Similar columns, with carboxylate groups as acceptors for water H atoms rather than peptide carbonyl groups, have been found for L-Asp-Gly·H_2O (Eggleston *et al.*, 1981), for L-Arg-L-Asp·$2H_2O$ (Rama-

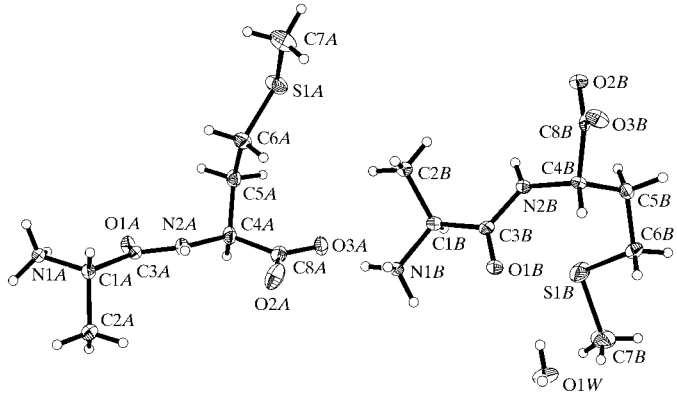


Figure 1
The asymmetric unit of L-Ala-L-Met, showing peptide molecules *A* and *B* and the solvent water molecule. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as spheres of arbitrary size.

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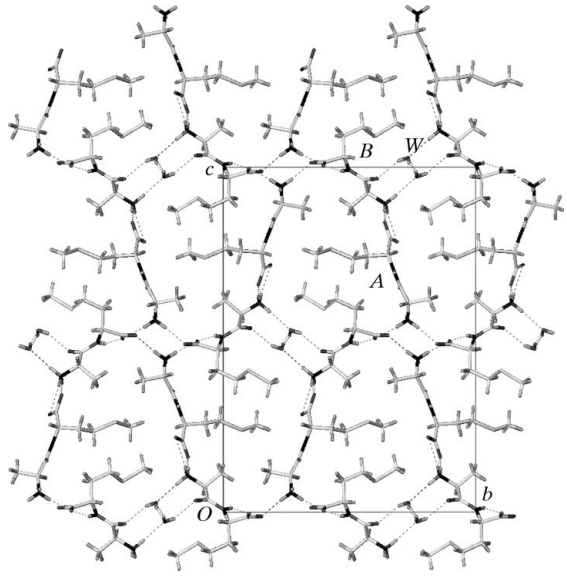

Figure 2
The molecular packing and unit cell viewed along the *a* axis. Molecules in the asymmetric unit are identified by the labels *A*, *B* and *W* (water).

krishnan & Viswamitra, 1988) and twice in the 1:1 complex L-His-L-Ser–Gly-L-Glu·6H_2O (Suresh & Vijayan, 1985). L-Pro-Gly (Narasimhan & Chacko, 1982) and L-Pro-Val (Narasimhan *et al.*, 1982) have polymer structures in which water molecules do not accept amine H atoms.

It was no surprise to find that the structure of AM is completely different from the monoclinic structure of D,L-Ala-L,D-Met (Stenkamp & Jensen, 1974; Guillot *et al.*, 2001), the difference being due to the different directions in which side chains are disposed relative to the main chain for L–L and D,L–L,D diastereomers (Görbitz & Etter, 1992).

The hydrogen-bond geometry is detailed in Table 2. All amine H atoms of molecule *A* are donated to molecule *B* carboxylate groups and *vice versa* (including a three-center interaction for atom H2*B*; Table 2), except for atom H1*B*, which is accepted by the water molecule. Neighboring molecules of type *A* or type *B* are connected by hydrogen bonds, with the N—H peptide bond as the donor, and by a number of weak interactions with C^{α}—H donors including C4*B*—H41*B*···S1*B* (Fig. 3). A search of the CSD revealed that C—H···S(L-Met) contacts are surprisingly ubiquitous, the shortest H···S distance being 2.85 Å. The most common donor is, however, not C^{α}—H as in AM, but the terminal methyl group of another L-Met side chain.

In summary, the hydrogen-bond network in AM incorporates two peptide molecules in the asymmetric unit, both with unusual L-Met side-chain conformations, together with a solvent water molecule that forms extended hydrogen-bonded polymers along the shortest crystallographic axis.

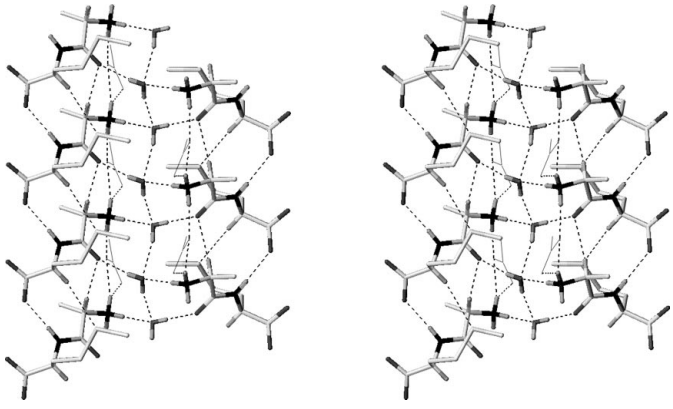

Figure 3
A stereoview of the chains of water molecules, related by twofold screw symmetry, along the *a* axis. Peptide *B* molecules surround the column. H atoms not involved in hydrogen bonds have been omitted for clarity. For peptide *A* molecules only line drawings of the carboxylate groups are included.

Experimental

The title compound was obtained from Bachem and used as received. Crystals were grown by slow diffusion of acetonitrile into an aqueous solution (30 µl) containing the peptide (∼1 mg).

Crystal data

$C_8H_{16}N_2O_3S·0.5H_2O$
M_r = 229.31
Orthorhombic, $P2_12_12_1$
a = 5.0809 (2) Å
b = 17.9228 (9) Å
c = 24.5005 (11) Å
V = 2231.11 (17) Å^3
Z = 8
D_x = 1.365 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 5401 reflections
θ = 1.7–27.1°
μ = 0.28 mm^{-1}
T = 105 (2) K
Needle, colorless
0.58 × 0.05 × 0.03 mm

Data collection

Siemens SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.829, T_{max} = 0.992
13 921 measured reflections
4661 independent reflections
3741 reflections with $I > 2\sigma(I)$
R_{int} = 0.099
θ_{max} = 27.1°
h = −6 → 6
k = −21 → 21
l = −31 → 31

Table 1
Selected geometric parameters (Å, °).

S1*A*—C7*A*	1.794 (3)	S1*B*—C7*B*	1.796 (3)
S1*A*—C6*A*	1.810 (3)	S1*B*—C6*B*	1.796 (3)
O1*A*—C3*A*	1.229 (3)	O1*B*—C3*B*	1.229 (3)
O2*A*—C8*A*	1.230 (3)	O2*B*—C8*B*	1.256 (3)
O3*A*—C8*A*	1.275 (3)	O3*B*—C8*B*	1.259 (3)
N1*A*—C1*A*	1.487 (3)	N1*B*—C1*B*	1.493 (3)
N2*A*—C3*A*	1.335 (3)	N2*B*—C3*B*	1.347 (3)
C7*A*—S1*A*—C6*A*	101.40 (14)	C7*B*—S1*B*—C6*B*	98.30 (14)
N1*A*—C1*A*—C3*A*—N2*A*	159.11 (19)	N1*B*—C1*B*—C3*B*—N2*B*	−175.58 (19)
C1*A*—C3*A*—N2*A*—C4*A*	173.8 (2)	C1*B*—C3*B*—N2*B*—C4*B*	178.65 (19)
C3*A*—N2*A*—C4*A*—C8*A*	−156.2 (2)	C3*B*—N2*B*—C4*B*—C8*B*	−124.4 (2)
N2*A*—C4*A*—C8A—O2*A*	0.2 (3)	N2*B*—C4*B*—C8*B*—O2*B*	−57.8 (2)
N2*A*—C4*A*—C5*A*—C6*A*	64.5 (3)	N2*B*—C4*B*—C5*B*—C6*B*	−74.5 (3)
C4*A*—C5*A*—C6*A*—S1*A*	152.83 (15)	C4*B*—C5*B*—C6*B*—S1*B*	71.8 (3)
C5*A*—C6*A*—S1*A*—C7*A*	178.66 (17)	C5*B*—C6*B*—S1*B*—C7*B*	−177.3 (2)

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0356P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.090$	$\Delta\rho_{max} = 0.29$ e Å^{-3}
$S = 0.99$	$\Delta\rho_{min} = -0.35$ e Å^{-3}
4661 reflections	Absolute structure: Flack (1983), 1893 Friedel pairs
290 parameters	Flack parameter = −0.04 (8)
H atoms treated by a mixture of independent and constrained refinement	

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1A—H1A···O2B^{i}	0.89	1.85	2.736 (2)	175
N1A—H2A···O2B^{ii}	0.89	2.32	2.815 (3)	115
N1A—H3A···O3B^{iii}	0.89	1.86	2.748 (2)	172
N2A—H4A···O1A^{iv}	0.81	2.58	3.346 (3)	158
C1A—H11A···O1A^{iv}	0.99	2.55	3.300 (3)	132
C4A—H41A···O2A^{v}	1.04	2.26	3.165 (4)	145
N1B—H1B···O1W^{vi}	0.92	2.03	2.950 (3)	177
N1B—H2B···O3A	0.92	2.07	2.937 (3)	157
N1B—H2B···O2A	0.92	2.25	3.024 (2)	141
N1B—H3B···O3A^{iv}	0.92	1.87	2.793 (3)	175
N2B—H4B···O3B^{v}	0.85	2.05	2.875 (3)	163
C1B—H11B···O1B^{v}	0.94	2.34	3.234 (3)	157
C4B—H41B···S1B^{iv}	0.99	3.05	3.901 (3)	145
O1W—H1W···O1W^{vii}	0.81 (3)	2.14 (3)	2.931 (2)	167 (3)
O1W—H2W···O1B	0.72 (3)	2.09 (3)	2.779 (3)	159 (3)

Symmetry codes: (i) $1-x, \frac{1}{2}+y, \frac{3}{2}-z$; (ii) $\frac{1}{2}-x, 1-y, z-\frac{1}{2}$; (iii) $\frac{3}{2}-x, 1-y, z-\frac{1}{2}$; (iv) $1+x, y, z$; (v) $x-1, y, z$; (vi) $x-\frac{1}{2}, \frac{3}{2}-y, 2-z$; (vii) $\frac{1}{2}+x, \frac{3}{2}-y, 2-z$.

Data were collected by measuring three sets of exposures (with the detector set at $2\theta = 29°$, and using a crystal-to-detector distance of 5.00 cm). The coordinates for the water H atoms, which were found in an electron-density map, were refined; other H atoms were placed geometrically and treated in the refinement with constraints. Free rotation of amine and methyl groups was permitted. U_{iso} values for H atoms were set at $1.2U_{eq}$ of the carrier atom, or $1.5U_{eq}$ for water, methyl and amine groups. The Flack (1983) parameter confirmed the known absolute structure; Friedel pairs were not merged in the final refinements.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

The purchase of the Siemens SMART CCD diffractometer was made possible through support from the Research Council of Norway (NFR).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1679). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. & Motherwell, W. D. S. (2002). *Acta Cryst.* B**58**, 407–422.
Bruker (1998). *SMART*. Version 5.054. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2000). *SHELXTL*. Version 6.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2001). *SAINT-Plus*. Version 6.22. Bruker AXS Inc., Madison, Wisconsin, USA.
Chen, C. & Parthasarathy, R. (1977). *Acta Cryst.* B**33**, 3332–3336.
Eggleston, D. S., Valente, E. J. & Hodgson, D. J. (1981). *Acta Cryst.* B**37**, 1428–1430.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Görbitz, C. H. (2002). *Acta Cryst.* B**58**, 849–854.
Görbitz, C. H. (2003*a*). *Acta Cryst.* C**59**, o589–o592.
Görbitz, C. H. (2003*b*). *New J. Chem.* **27**. In the press.
Görbitz, C. H. & Etter, M. C. (1992). *Int. J. Peptide Protein Res.* **39**, 93–110.
Görbitz, C. H. & Gundersen, E. (1996). *Acta Cryst.* C**52**, 1764–1767.
Guillot, R., Muzet, N., Dahaoui, S., Lecompte, C. & Jelsch, C. (2001). *Acta Cryst.* B**57**, 567–578.
Narasimhan, P. & Chacko, K. K. (1982). *Cryst. Struct. Commun.* **11**, 695–700.
Narasimhan, P., Chacko, K. K. & Swaminathan, S. (1982). *Cryst. Struct. Commun.* **11**, 2051–2056.
Ramakrishnan, B. R. & Viswamitra, M. A. (1988). *Acta Cryst.* C**44**, 1959–1961.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Stenkamp, R. E. & Jensen, L. H. (1974). *Acta Cryst.* B**30**, 1541–1545.
Suresh, C. G. & Vijayan, M. (1985). *Int. J. Peptide Protein Res.* **26**, 329–336.
Valle, G., Guantieri, V. & Tamburro, A. M. (1990). *J. Mol. Struct.* **220**, 19–24.